Diagnosis and Management of Soft-tissue Masses

Abstract
Soft-tissue masses of the extremities are common entities encountered by nearly all providers of musculoskeletal patient care. Proper management of these lesions requires a specific process of evaluation. A detailed history and physical examination must be performed. Appropriate imaging studies must be obtained based on clinical indications. MRI is the imaging modality of choice for diagnosis of soft-tissue masses, with CT and ultrasonography used as secondary options. These modalities aid the clinician in developing an appropriate differential diagnosis and treatment plan. When the initial evaluation is inconclusive, biopsy must be performed. A diagnosis must be established before definitive treatment with surgical excision or, in rare cases, radiation therapy is performed. Clinicians without significant experience in treating soft-tissue masses should consider referral to a musculoskeletal oncologist for specialized care when a definitive diagnosis of a benign lesion cannot be made. Several studies have shown that multidisciplinary care in specialized referral centers optimizes outcomes and diminishes comorbid complications.

Epidemiology
Soft-tissue masses are commonly encountered by both primary care physicians and surgeons. Benign soft-tissue masses outnumber malignant tumors approximately 150:1, with approximately 20 malignant soft-tissue masses per 1 million people in the United States. Orthopaedists must recognize the unique characteristics of benign and malignant soft-tissue masses to determine which masses require further evaluation. Adherence to a specific process of evaluation and management of these soft-tissue masses is critical for optimal patient outcomes.

Clinical Presentation and Evaluation
A comprehensive history and physical examination, with appropriate cross-sectional imaging and a review
of histologic material (when indicated), are essential for diagnosis of soft-tissue masses. In general, an accurate differential diagnosis can be formulated after the history and physical examination. Appropriate imaging can help narrow the differential diagnosis, and histologic analysis will typically confirm it (Table 1).

It should be noted that most soft-tissue neoplasms, whether benign or malignant, present as painless masses. Many healthcare providers believe that only painful masses are worrisome. This myth must be laid to rest. Soft-tissue sarcomas typically cause pain only if they compress neurologic structures or become massive in size (>10 cm). Soft-tissue masses can be stable in size or can grow slowly or rapidly. An unrelated trauma can often draw attention to an existing mass. Pertinent questions include the following: How long has the mass been present? Is it painful? Is there any history of trauma or prior history of cancer? Are there any concurrent symptoms? Stability over time favors a benign diagnosis because sarcomas typically grow rapidly over a period of weeks to months. Rarely, sarcomas (synovial sarcoma in particular) can be stable for long periods of time before enlarging. Pain is fairly rare except in specific situations. Pain, especially with activity, is also common with hemangiomas. Trauma may result in the development of myositis ossificans or a calcified hematoma. Prior malignancy may have required radiation therapy, which can predispose the patient to develop a soft-tissue sarcoma. This tumor rarely presents with systemic signs such as fevers, chills, and night sweats. Waxing and waning size is commonly seen with ganglions and hemangiomas, but it is not characteristic of sarcomas.

The size, depth, consistency, and mobility of the mass are also important for narrowing the diagnosis. A mass that is large (>5 cm), deep (in relation to investing fascia), and firmer than the surrounding muscle should raise suspicion for a malignancy. Small, superficial masses are more likely to be benign, with the caveat that up to 32% of soft-tissue sarcomas can present this way. A fixed mass may suggest an underlying bony origin or a more infiltrative lesion (eg, desmoid tumor). A consistency softer than muscle (often described as “doughy”) is a characteristic of lipomas, whereas masses that are extremely firm and fixed are commonly desmoid tumors. Superficial ecchymosis is often seen with traumatic hematoma because it tracks along fascial planes. Bleeding within a tumor is often contained within the tumor capsule and rarely reaches the superficial tissues. Several specific findings can narrow the differential diagnosis even further. Ganglion cysts may transilluminate with a pen light; vascular lesions (eg, hemangiomas, arteriovenous malformations) may have bruits or palpable thrills. Peripheral nerve sheath tumors may have a positive Tinel sign or pain with compression.

### Table 1

<table>
<thead>
<tr>
<th>Characteristics of Select Soft-tissue Tumors and Appropriate Diagnostic Imaging</th>
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<tr>
<td>Mass</td>
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</tr>
<tr>
<td>Lipoma</td>
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<tr>
<td>Hemangioma/lymphangioma</td>
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<tr>
<td>Abscess</td>
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<tr>
<td>Myositis ossificans</td>
</tr>
<tr>
<td>Ganglion cyst</td>
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<tr>
<td>Schwannoma</td>
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<tr>
<td>Desmoid</td>
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<tr>
<td>Pigmented villonodular synovitis</td>
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<tr>
<td>Sarcoma</td>
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Dr. Mayerson or an immediate family member has received research or institutional support from Millennium Pharmaceuticals and serves as a board member, owner, officer, or committee member of the American Orthopaedic Association, the Musculoskeletal Tumor Society, the National Comprehensive Cancer Network, and the Ohio Orthopaedic Society. Dr. Lewis or an immediate family member has received research or institutional support from Stryker and serves as a board member, owner, officer, or committee member of the American Academy of Orthopaedic Surgeons and the Western Orthopaedic Association. Dr. Morris or an immediate family member serves as a board member of the American Academy of Orthopaedic Surgeons and the Western Orthopaedic Association. Dr. Scharschmidt or an immediate family member has received anything of value from or has stock or stock options held in a commercial company or institution related directly or indirectly to the subject of this article.
Regional lymph nodes should be palpated. In the setting of reactive or neoplastic masses, the lymph nodes may be enlarged. Synovial sarcoma, epithelioid sarcoma, rhabdomyosarcoma, clear cell sarcoma, and alveolar soft part sarcoma are among the subtypes that are known to spread to the lymph nodes.

After the history and physical examination, the orthopaedic surgeon can decide whether to proceed with imaging and/or biopsy. Findings that warrant continued conservative observation include a small, superficial mass that is doughy and consistent with lipoma; a mass with changes in size (increase and decrease) consistent with a ganglion cyst or intramuscular hemangioma; and a mass that initially develops after trauma. Any mass >5 cm that is firm and deep should be considered a malignancy. If the diagnosis is in question, additional workup with imaging and/or biopsy should be performed.

**Laboratory Studies**

There are no specific laboratory studies that are of significant benefit in the evaluation of soft-tissue masses. Infectious processes can manifest with an elevated white blood cell count, erythrocyte sedimentation rate, and C-reactive protein level. Lactate dehydrogenase levels can be elevated in the setting of small round blue cell tumors. Calcium and phosphorus levels can be abnormal in the setting of tumoral calcinosis, and uric acid levels can be elevated in patients with gout. In general, these tests are nonspecific and are of limited use for evaluation of soft-tissue tumors.

**Imaging**

Imaging is best performed using a multimodality approach. Initial evaluation typically includes radiography and MRI. MRI offers the best delineation of the soft-tissue structures, elucidation of the relationship of the mass to neurovascular structures, and a glimpse into the intratumoral environment. However, other imaging modalities, such as radiography, ultrasonography (US), CT, and positron-emission tomography with CT (PET-CT) may offer important clues to the diagnosis.

Radiography has a limited role in the diagnosis and staging of soft-tissue tumors, but it is quick, inexpensive, and offers important clues to the origin and differential diagnosis of a soft-tissue mass. Although small, deep-seated soft-tissue tumors are often difficult to recognize on radiography, larger tumors often distort the soft-tissue planes and may produce a local prominence at the surface (Figure 1).

Radiography can demonstrate the distortion of tissue planes; radiolucent fatty areas; indolent or aggressive remodeling of bone; radiolucent foreign bodies, which often cause a reactive soft-tissue mass; and soft-tissue calcification or ossification. Several readily evident features on radiography can help narrow the diagnosis, including calcified phleboliths (hemangiomas); a cumulus cloud-like appearance (extraskeletal osteosarcoma); and mature peripheral trabecular bone (myositis ossificans).

MRI is considered the imaging modality of choice for localization, characterization, and staging of soft-tissue tumors. It is highly sensitive and accurately demonstrates the anatomic location of the mass and its relationship to the adjoining neurovascular structures and bone. MRI provides superb contrast detail of various soft-tissue elements (eg, fat, muscle, bone). However, it is inferior to plain radiography and CT for detection of soft-tissue calcifications, osseous infiltration, and the presence of air. Different pulse sequences highlight specific tissue characteristics. The standard MRI sequences used to evaluate a soft-tissue tumor include axial and coronal T1- and T2-weighted sequences, fat saturation, and T1-weighted sequences with contrast. These sequences provide the best means of determining the anatomic orientation of the mass. T1-weighted MRI allows for excellent anatomic visualization, given its high spatial resolution. T2-weighted MRI shows abnormal changes, free extracellular water, and tissue edema. Fat suppression techniques subtract the signal produced by adipose tissue and highlight abnormal changes and tissue edema (even more than do conventional T2-weighted images).

Soft-tissue sarcomas tend to grow by centrifugal extension and tend to respect anatomic planes. They often appear encapsulated and have a characteristic heterogeneous appearance on
T1- and T2-weighted sequences. Most soft-tissue tumors are hypointense on T1-weighted images, hyperintense on T2-weighted images, and show central enhancement on post-contrast magnetic resonance images. Fat suppression sequences can confirm the presence of a fat-containing lesion such as that seen in some liposarcomas. These lesions often contain areas of necrosis, which impart a heterogeneous appearance on T2-weighted sequences, short tau inversion recovery, and post-contrast T1-weighted sequences.

Gadolinium-enhanced imaging has become an important part of the workup for soft-tissue masses because it allows the clinician to differentiate between cystic and solid lesions. Cystic lesions have rim enhancement, which is not present in solid lesions (Figure 2). This is especially important for differentiating between myxomas, myxoid liposarcoma, and fluid-filled cysts. All have a similar appearance on spin-echo and T1- and T2-weighted sequences; however, when gadolinium contrast is administered, the cystic lesion will have rim enhancement, while a myxoid liposarcoma will have heterogeneous enhancement within the mass, and a myxoma will demonstrate homogeneous enhancement throughout. Gadolinium also facilitates the detection of small tumor nodules in predominantly cystic lesions or spontaneous hematomas. The small tumor nodule will show enhancement within the normally homogeneous cystic lesion or hematoma. In addition, gadolinium-enhanced MRI is helpful for assessing treatment response. It can be used to differentiate viable tissue from non-viable or necrotic tissue within the tumor. Gadolinium can also be used to guide needle biopsy, aiding the clinician in distinguishing a recurrent tumor or viable residual tumor tissue from granulation tissue in the surgical bed. In contrast to the delayed enhancement seen with granulation tissue, viable residual tumor tissue displays vivid and early enhancement with contrast.

Short tau inversion recovery sequences are a type of fat-suppressed T2-weighted magnetic resonance image that highlights areas of increased fluid and/or edema even more than conventional T2-weighted techniques. Gradient-echo sequences provide excellent visualization of hemorrhage or hemosiderin deposition and tend to be the sequence of choice in the setting of suspected vascular lesion, hematoma, or pigmented villonodular synovitis. MRI helps the clinician generate a differential diagnosis and an appropriate treatment plan for the patient with a soft-tissue mass. However, it has a limited ability to provide specific tissue diagnosis except in the case of lipomas, ganglion cysts, peripheral nerve sheath tumors, and hemangiomas (Figure 3).

US is a relatively inexpensive and accessible tool that also can be used to aid diagnosis of soft-tissue tumors. As a first-line imaging modality, US is sensitive for the detection and evaluation of soft-tissue masses, especially focal superficial lesions. US can aid the clinician in differentiating between solid and often benign cystic masses and can be used to establish the shape of the lesion, compressibility, and vascularity as well as the presence of calcifications and the pattern of internal echoes. These features can be helpful when establishing a differential diagnosis. When combined with Doppler, US can be particularly helpful for assessing the blood flow within

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**Figure 2**

Axial (A and B) and sagittal (C) T1-weighted gadolinium-enhanced magnetic resonance images of the right thigh in a 52-year-old man demonstrating a mass with rim-enhancing characteristics only. The arrows demonstrate a solid component with heterogeneous enhancement, indicating a cystic lesion with solid components that raise suspicion for sarcoma.
a lesion (Figure 4). This is particularly important for determining whether a mass represents a scar or a small soft-tissue tumor. For this reason, clinicians often use US to evaluate for recurrence. This modality is also useful for detecting retained foreign bodies that, when small, can elicit a reaction that mimics a soft-tissue tumor. This is especially helpful in young children, who are more prone than adults to have retained foreign objects, and in those who may have difficulty tolerating MRI.

The role of CT for diagnosis of soft-tissue masses has diminished as the role of MRI has evolved. CT is typically used as an adjuvant to MRI and is often used because of its shorter examination times and superior patient tolerance (not as enclosed as MRI). It is often the imaging modality of choice for patients who cannot undergo MRI, including those with pacemakers or indwelling cardiac stents and those who are too large to fit in the MRI scanner.

CT is useful for evaluating four characteristics of soft-tissue masses: mineralization patterns, lesion density, bone involvement, and vascular involvement. Mineralization within a soft-tissue mass can be the result of calcification or ossification. Unlike MRI, which is limited in the setting of mineralization secondary to the variable signal intensity of calcium, CT may be able to distinguish calcification from ossification. Ossification is marked by trabecular bone formation that may be discernible on CT. This is particularly true in the setting of heterotopic ossification; CT can reveal the characteristic peripheral ossification and the inner trabecular pattern of mineralization. When soft-tissue tumors generate an osteoid or chondroid matrix, the distinct mineralization pattern seen on CT often helps the clinician establish the differential diagnosis. On CT, a cloud-like pattern with increasing density toward the center or a ground-glass pattern can be typical of an osteoid matrix, whereas calcifications in rings and arcs (often with dense punctate) or stippled calcifications suggest chondroid lesions.

CT is also useful for differentiating lesions based on tissue density. For example, fat has a specific appearance on CT due to its density. The location of fat within a tumor can also offer clues to other types of lesions that contain fat or have fat associated with the mass. Lesions that contain fluid have a certain density and, when intravenous contrast is used, the enhancement can aid the clinician in establishing a differential diagnosis. Rim enhancement without internal enhancement is a characteristic of true cystic lesions such as ganglion cysts, seromas, or synovial cysts. In addition, CT angiography can be useful for illuminating the vascular supply or inner vascularity of a lesion, which can aid diagnosis and preoperative planning.

PET, most commonly used in conjunction with CT (PET-CT), provides precise anatomic correlation of tumors and information about metabolic activity within a soft-tissue tumor. PET-CT detects positron emission decay from an administered radioisotope, and generates an image of the entire body. F-18 fluorodeoxyglucose is the agent commonly used; it is tagged with proton-emitting radioactive fluorine, which behaves like glucose and reflects metabolic activity in the body but does not decay further. The proton-emitting metabolite trapped within cells allows subsequent imaging by emitting two 512 keV gamma energy photons perpendicular to each other. The amount of radiotracer activity within the cells reflects the metabolic activity. Typically, high-grade malignant soft-tissue tumors have high rates of glucose metabolic activity. They show increased F-18 fluorodeoxyglucose uptake compared with the uptake of benign or low-grade
soft-tissue malignant tumors. Although PET-CT is not used for initial evaluation of soft-tissue sarcoma, it has been found to be useful to assess treatment response after systemic therapy or to identify recurrence in a previously radiated bed.9

Management

Management of a soft-tissue mass is based on the underlying diagnosis. For many benign tumors, observation is sufficient. When surgical intervention is indicated, most benign masses are removed with a marginal excision. Malignant soft-tissue tumors require a multimodality approach. Once a diagnosis of sarcoma is established, decisions regarding the need for adjuvant treatment (radiation therapy and/or chemotherapy) must be coordinated with surgery to remove the tumor. Surgical management of malignant tumors is undertaken with the goal of achieving wide margins. The three key aspects of surgical management of soft-tissue tumors are the biopsy, oncologic resection, and unplanned oncologic excision.

Biopsy

Many physicians consider biopsy to be a simple, low-risk procedure. Although the procedure is not technically demanding, complications are common and can ultimately compromise the final surgical outcome. In a study of complications following a biopsy performed by a non-oncologic surgeon, the Musculoskeletal Tumor Society reported a complication rate of 19% in 597 biopsies performed at a referring institution; this rate was 12-fold greater than that of biopsies performed by an orthopaedic oncologist.10 The complications included 18 unnecessary amputations. Biopsy planning requires a full understanding of the treatment options and knowledge of the limb salvage incisions as well as access to an experienced musculoskeletal pathologist and complete imaging. The biopsy should be viewed as the first step of a successful limb salvage operation.

Needle and open biopsies are the two main types of biopsy for soft-tissue tumors. Needle biopsies are further subclassified as fine-needle aspiration and core. Fine-needle aspiration biopsy offers several advantages: it is easily done in the office, does not require local anesthesia, has limited soft-tissue contamination, can be processed in minutes (if the pathologist is available), and is relatively inexpensive. Core needle biopsies use a large-bore hollow needle to obtain a 1.5-cm sliver of tissue. Local anesthesia is required and several passes of the needle are typically performed. For easily palpable masses, biopsies can be done in the office, whereas deeper biopsies are best performed with image guidance. Although all needle biopsies are cost-effective, with manageable contamination, the accuracy of tumor grade and histology subtype varies and is highly dependent on the pathologist’s experience as well as the amount of tissue available for ancillary studies such as immunohistochemical staining and cytogenetics.10-15 Liu et al15 described guidelines for image-guided biopsies.

Open biopsies can be subclassified as incisional or excisional. In an incisional biopsy, a portion of the tumor is removed to make a diagnosis. The incision should be placed along the limb salvage incision or just parallel to it such that the entire tract can be ellipsed en bloc at the time of definitive surgery. Excisional biopsy implies a planned marginal resection of the mass. This type of biopsy is best reserved for masses that are thought to be benign such as a lipoma or peripheral nerve sheath tumor. In a primary wide excision, the entire mass is removed along with a cuff of normal tissue. Typically, this technique is reserved for small,
indeterminate lesions. The decision to perform a primary excision of a malignant mass is best made by an orthopaedic oncologist. Although excisional biopsy has the highest level of diagnostic accuracy, it is associated with the most morbidity if the malignancy is not completely removed. Table 2 summarizes the types of biopsy for soft-tissue masses and their key points.

Because soft-tissue masses are so common, surgeons of every subspecialty may encounter them. Table 3 summarizes the key surgical principles to observe when surgical management is required and an orthopaedic oncologist is unavailable. In addition to these principles, it is important that the clinical suspicion match the imaging results. If some aspect of the imaging does not make sense, the clinician should not proceed.

**Oncologic Resection**

Classification of oncologic resection is as follows: intralesional, marginal, wide, and radical excision (Figure 5). Intralesional excision is typically performed by entering the substance of the tumor and removing it in a piece-meal fashion. Intralesional excision is reserved for benign conditions such as a hematoma. Marginal excision refers to en bloc excision through the reactive zone. The reactive zone refers to the thin capsule around a lipoma or the signal changes seen surrounding a mass on MRI. Marginal excision is also reserved for benign tumors such as neurofibromas, lipomas, and giant cell tumors of the tendon sheath. Marginal excision is not indicated for malignancies because tumor cells may be present within the reactive zone.17 Wide excision is most commonly performed for primary malignant masses. In a wide excision, a cuff of normal tissue is removed as the margin to ensure complete removal of the tumor. Greater than 90% of extremity sarcomas can be widely excised, preserving the limb. Amputation is performed when it is impossible to achieve negative/free margins or when function would be superior with amputation rather than limb salvage. Radical resection refers to the removal of an entire compartment. For example, a mass located in the tibialis anterior muscle would require resection of all of the muscles of the anterior compartment to obtain a radical resection. In an overwhelming percentage of cases of high-grade sarcoma, chemotherapy and/or radiation therapy are used as adjuvant treatment modalities to allow limb salvage surgery. With the use of these modalities, radical resections are rarely performed and are reserved for multifocal tumors or tumors large enough that the compartment would no longer be functional after resection of the sarcoma.

**Unplanned Oncologic Excision**

Despite educational efforts among the various surgical societies, unplanned or inadvertent sarcoma excision still occurs. The primary reasons for

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**Table 2**

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<thead>
<tr>
<th>Biopsy</th>
<th>Definition</th>
<th>Key points</th>
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<tr>
<td>Needle (fine-needle</td>
<td>Placement of a needle into a mass to obtain diagnostic tissue</td>
<td>May be done in the office or by an interventional radiologist, low morbidity, may not obtain enough tissue for ancillary studies (cytogenetics, immunohistochemical staining)</td>
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<td>aspiration and core)</td>
<td></td>
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<tr>
<td>Open incisional</td>
<td>Diagnostic tissue is obtained through an open surgical incision.</td>
<td>Limb salvage incision should be drawn first. A larger tissue sample allows for molecular diagnostic testing. Any tissue exposed during open biopsy must be removed during definitive surgery (vessels, nerves). Poorly placed biopsy sites may adversely affect the surgeon’s ability to resect the tumor without significantly increased morbidity and a substantial increased risk of adverse outcomes that include amputation.10</td>
</tr>
<tr>
<td>Open excisional</td>
<td>Removal of the entire tumor as the biopsy</td>
<td>Typically reserved for masses &lt;3 cm, those thought to be benign, or when the contamination associated with biopsy is considerable; best done by a musculoskeletal oncologist; associated with significant morbidity when a malignancy is incompletely excised</td>
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inadvertent excision include lack of or inadequate imaging before the procedure or inappropriate interpretation of imaging studies. The outcomes of unplanned excision vary. Some series report increased local recurrence and worse overall survival in the re-excision group, whereas others note minimal impact on these two parameters. However, consensus exists with regard to the increased morbidity associated with complex soft-tissue coverage performed with re-excision.

When contemplating removal of a soft-tissue mass, the surgeon must consider that the final pathology report may demonstrate malignancy. Therefore, the use of sound surgical principles for tumor excision is crucial to minimize contamination. If the diagnosis is in question at the time of surgery, a frozen section should be obtained to evaluate for malignancy. If a potential tumor is discovered intraoperatively, a tissue sample should be obtained, with care taken to ensure that a sufficiently large sample is obtained to establish a diagnosis. Unrequired dissection or exposure could lead to further contamination and should be avoided.

All physicians involved in the care of the patient with a musculoskeletal soft-tissue mass must be familiar with the surgical principles for management of soft-tissue masses. The limb salvage incision should be drawn first. If the surgeon does not know the incision, the biopsy should not be done. Transverse incisions should be avoided. If local anesthesia is used, it should be done in a direct line with the needle tract so as to cover as little area as possible. The most direct approach to the tumor should be taken. Do not develop intermuscular planes or expose critical neurovascular structures. Do not develop flaps. Meticulous hemostasis must be maintained; hematomas contain tumor cells and are considered contaminated. If a tourniquet is used, gravity exsanguination only should be employed; do not use compressive bandages. If a drain is needed, it should exit in line with the incision such that the drain tract and site can be easily incorporated into the definitive incision. Open biopsy should be avoided in high-risk areas such as the axilla, popliteal fossa, and carpal tunnel where wide contamination may lead to amputation. Arthroscopy is not indicated as a planned primary method of biopsy for an intra-articular soft tissue mass.

### Table 3

**Surgical Principles for Management of Soft-tissue Masses**

<table>
<thead>
<tr>
<th>Principle</th>
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<tr>
<td>The limb salvage incision should be drawn first. If the surgeon does not know the incision, the biopsy should not be done. Transverse incisions should be avoided.</td>
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Illustration demonstrating the surgical resection margins accepted by the Musculoskeletal Tumor Society as originally described by Enneking and Dunham. Only soft-tissue structures are resected or excised with these margins.
natural history and presentation of various soft-tissue masses, physical examination findings, reasons for obtaining advanced imaging (indicated for all masses >5 cm superficial to fascia, all masses deep to fascia, or any soft-tissue mass with new onset rapid growth), and the appropriate imaging modality for each clinical circumstance. Attention to these details is essential to formulate an appropriate differential diagnosis. When clinically indicated, referral to oncologic specialists for management is appropriate. In the setting of large, deep lesions, careful triage is essential because these are the most difficult masses to treat and have the greatest risk of complications after unplanned surgical treatment. All biopsy principles must be followed to diminish the possibility of harm to the patient. Proper referral to a musculoskeletal oncologist can optimize the outcome of the limb and the patient.

Summary

Proper management of soft-tissue masses requires the use of a specific process for evaluation and management. This process includes a thorough history and physical examination as well as imaging studies. MRI is commonly used for diagnosis of these tumors, with CT and US used as secondary imaging modalities. Imaging is essential for developing a proper differential diagnosis and treatment plan. If the diagnosis remains unclear following the initial evaluation, biopsy can be performed. If a definitive diagnosis proves elusive, the clinician should consider a referral to a musculoskeletal oncologist. The multidisciplinary care provided by specialized treatment centers has been shown to optimize outcomes and diminish complications.

References

Evidence-based Medicine: Levels of evidence are described in the table of contents. In this article, references 13, 16, and 17 are level I studies. References 3, 11, 12, 18, and 19 are level II studies. References 20 and 21 are level III studies. References 2, 5-10, 14, and 15 are level V expert opinion.

References printed in bold type are those published within the past 5 years.


